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THE VALUE OF TROPONIN I IN THE DIAGNOSIS OF MYOCARDIAL INFARCTION AND OUTCOME IN SUDANESE PATIENTS

By

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LIST OF ABBREVIATIONS

AMI	Acute myocardial infarction.
CK	Creatine kinase.
cTnI	Cardiac troponin I.
cTnT	Cardiac troponin T.
LD	Lactate dehydrogenase.

ABSTRACT

This is a prospective study conducted at Elshaab Teaching Hospital in the period between May and July 2005.

In this study 60 patients presented with acute chest pain to the cardiology department. Special selection criteria were considered, and any patient presented with acute chest pain, not for more than two weeks, and not traumatic was included.

The objectives of the study were to determine the value of troponin in the diagnosis of myocardial infarction and risk stratification.Troponin I concentration was measured at presentation and the patients were followed up for 1 month.

The study concluded that troponin is statistically significant in diagnosing myocardial infarction and acute coronary syndrome, where 33.3% of the patients had a troponin concentration >1.0ng/mL, 20.0% had acute myocardial infarction and 5.0% had unstable angina.

There was no significant relation between duration of chest pain and troponin concentration and the outcome related to the troponin concentration was approaching significance where 20.0% of the patients with a troponin concentration >1.0ng/mL passed away, and 10.0% had another infarct.

This study recommended that patients presenting with acute chest pain should be diagnosed and risk stratified by using serial troponin measurement beside the clinical

and ECG findings. It also recommended that larger studies should be conducted to evaluate the relation between the time of presentation and the outcome with the Troponin I concentration.

ملخص الأطروحة

هذه الدراسة أجـــريت في مستشفي الشعب التعليمي في الفـــترة من أول مـــــايو وحتى أول يوليو 2005م.

شملت هذه الدراسة 60 مريضا" حضروا إلى المستشفى بقسم إمراض القلب يشتكون من الم حاد بالصدر.اعتبرت مقاييس اختيار خاصة بحيث أن أي مريض يعاني من الم حاد بالصدر، لا تزيد مدته عن أسبوعين، وليس بسبب إصابة قد ادخل في الدراسة.

. في تشخيص الذبحة الصدرية و الناتج عنها Troponin Iكانت الهداف من هذه الدراسة هي تحديد قيمة أل Troponin I تم فحص قيمة و تبعت حالة المريض لمدة شهر.

Troponin I أظهرت النتائج إن Troponin I يشخص الذبحة الصدرية حيث ان33.3 من المرضى كان مستوي

. كانت Unstable angina1.0 و 20.0% كانوا يعانون من الذبحة الصدرية و 5% من ng/mL اعلي من I هذه النتائج ذات دلالة احصائية.

. كادت العلاقة مع الناتج ان تكون ذات Troponin I لم تظهر الدراسة دلالة احصائية بين مدة السالم وتركيز ال 1.0 لديهم قد توفوا و 10.0% Troponin I ng/mL >دلالة حيث ان 20.0% من المرضى الذين كان مستوي اصيبوا بذبحة آخري.

Troponin وصت هذه الدراسة بان يشخص المرضي الذين يعانون من الم في الصدر بواسطة فحص ال مع Troponin I . كما أوصت بإقامة دراسات أوسع لدراسة علاقة الECGبجانب الفحص ألسريري و ال I زمن الحضور ألي المستشفي والناتج من الذبحة الصدرية

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CHAPTER ONE

Introduction

The heart is the muscular organ responsible for pumping blood to all parts of the body. Through rhythmic contractions, the right side pumps blood to the lungs to be oxygenated. The left side receives the oxygenated blood and pumps it to all parts of the body.

Heart is an efficient and durable pump. Anemia, arrhythmias, infection, and pulmonary embolism, can all precipitate heart failure but only myocardial infarction can be diagnosed by laboratory tests. Acute Myocardial Infarction (AMI) is gross necrosis of the myocardium as a result of interruption of the blood supply to the area, it is almost always caused by atherosclerosis of the coronary arteries upon which coronary thrombosis is superimposed[1].

The coronary arteries supply oxygenated blood to the heart muscle fibers. The coronary circulatory system consists of right and left coronary arteries. The right coronary artery arises from the right coronary sinus and courses through the right side of the atrioventricular groove, giving off vessels that supply the right atrium and the right ventricle. The vessel usually continues as the posterior descending coronary artery, which runs in the posterior interventricular groove and supplies the posterior part of the interventricular septum and the posterior left ventricular wall. The left coronary artery arises from the left coronary sinus. The first part is known as the left main coronary artery. It then divides into the left anterior descending and the left circumflex arteries. The left anterior descending artery runs in the anterior interventricular groove and supplies the anterior septum and the anterior left ventricular wall. The left circumflex artery travels along the left atrioventricular groove and gives off branches to the left atrium and ventricle. The sinus node and the AV node are supplied by the right coronary artery.

The cardiac fibers are composed of the cardiac specific contractile proteins-actin and myosin- and the regulatory proteins-troponin and tropomyosin. They also contain proteins and enzymes that are necessary for energy use, such as myoglobin, creatine kinase (CK), and lactate dehydrogenase (LD).Each of these proteins can be a marker for AMI[1].

The cardiac conducting system is viewed through the electrocardiogram (ECG). ECG identifies anatomical, metabolic, ionic, and hemodynamic changes of the heart. It presents a visible record of the heart's electrical activity. A normal ECG consists of P, QRS, and T wave. The P wave reflects the atrial contraction, the QRS the ventricular contraction and the T wave the electrical recovery of the ventricles.

PATHOGENISIS OF CORONORY ARTERY SYNDROMES

Atherosclerosis is the major cause of coronary artery syndromes which includes unstable angina and myocardial infarction. It causes plague formation in large and medium sized vessels. As the plague enlarges, it protrudes into the vessel's lumen and narrows it, so reducing the blood flow. The plague is composed of lipid, cell debris, smooth muscle cells, collagen, and calcium. It is covered by a fibrous cap.

Patients with involvement of the coronary arteries experience chest pain and shortness of breath with mild exertion. This is known as **angina**. It is due to ischemia. It is reversible and relieved by rest and vasodilating drugs and so is called **stable angina**.

Sometimes the fibrous cap ruptures and provokes thrombus formation in the vessel's lumen. If the vessel is completely blocked and there are no sufficient collaterals, acute myocardial ischemia and infarction occurs. If the occlusion is partial milder ischemia and myocardial damage known as **unstable angina** occurs. If this is not treated it will progress to AMI in 10% of patients.

Many conditions increase the risk of atherosclerosis. These include genetics, male sex, sedentary life style, hypertension, smoking, hyperlipidemia, and diabetes mellitus. The identification and treatment of individuals who may be at high risk for atherosclerosis can prevent or delay the progression of this disease. These patients are advised to eat healthy food, encouraged to exercise, discouraged from smoking and advised to treat high blood pressure and diabetes[2].Those with hyperlipidemia should reduce their weight if they are obese. If the hyperlipidemia persists then drug therapy is initiated.

Acute myocardial infarction occurs when blood flow to an area is suddenly blocked, and massive cell death ensues. The damaged cardiac cells release enzymes into the circulation. If the occlusion is complete for at least 15 to 20 min then the damage is irreversible and the necrotic area is replaced by nonfunctional fibrous tissue.

Acute myocardial infarction is characterized by acute central chest pain, lasting >20 min, often associated with nausea, sweating, dyspnoea and palpitations. When occlusion is sustained fro 4 to 6 hours the damage is maximal but most of it occurs within the first 2 to 3 hours. Restoration of blood flow in the first 4 to 6 hours is associated with salvage of the myocardium but best results are achieved if restoration occurs in 1 to 2 hours. Lysis of the coronary thrombus occurs spontaneously in about 50% of cases within 10 days[1]. In the case of chronic reduced blood flow, the damage is less significant because collaterals have developed. An infarction involving the whole thickness of the myocardium is called a transmural infarction[1].Patients who exhibit minimal myocardial damage may have experienced early spontaneous lysis, which accounts for many cases of nontransmural infarction[1].

PRECEPITATING FACTORS

In the majority of cases no precipitating factor is identified, however the event is not random. Studies have shown that AMI is more frequent during physical exercise, after surgical procedures, in the winter months, and during emotional stress. Trauma may also precipitate AMI by causing myocardial contusion and hemorrhage, or injury to the coronary arteries.

The early morning peak in AMI parallels the peak incidence of death from ischemic heart disease, occurring at about 0800 to 0900 hours. A second peak occurs at about 1700 hours. The reason this event occurs more often in the morning may be due to normal circadian rhythms. During the early morning, adrenergic activity, plasma fibrinogen levels, and platelet adhesiveness all increase naturally. Non transmural infarction does not exhibit this circadian rhythm.

CLINICAL HISTORY

The first symptom is usually angina occurring at rest, fatigue or shortness of breath. Then the pain becomes severe and prolonged, usually lasting for more than 30 minutes and frequently for many hours. It is described as being crushing or constricting, but may be characterized as stabbing or burning discomfort. It is retrosternal and can radiate to both sides of the chest or shoulders, favoring the left side. In some instances the pain is felt in the epigastrium and can be misdiagnosed as indigestion. Unlike angina the pain is not relieved by rest.

DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION

The World Health Organization (WHO) diagnosis of AMI requires two of the followings:

-History of chest pain

-ECG changes

-Elevation of cardiac markers.

When the ECG is not diagnostic cardiac markers are used[1].

ELECTROCARDIOGRAM

It is the cornerstone of diagnosis of acute myocardial infarction, so the first to be done. It shows changes due to ischemia, injury, and cell death reflected by T waves and ST segment changes and the appearance of an enlarged Q wave.

However clear cut differentiation may not be possible in every case. These specific patterns may sometimes be obscured by previous cardiac disease, or they may not appear at all.[1] If the ECG pattern is equivocal, then the physician must depend on serum markers for myocardial damage.

CARDIAC MARKERS

A **cardiac marker** is a clinical laboratory test useful in the detection of acute myocardial infarction or minor myocardial injury[3].

An ideal marker should fulfill the following criteria:

- ✓ It should be absolutely cardiac specific to allow reliable diagnosis in the presence of skeletal muscle injury.
- ✓ It should be highly sensitive to detect even minor damage to the heart.
- ✓ The marker should be able to differentiate between reversible and irreversible damage.

- ✓ In acute myocardial infarction, it should allow monitoring of reperfusion therapy and the estimation of the infarct size and prognosis.
- ✓ It should be stable and the measurement rapid, easy to perform, quantitative, and cost effective.

At this point it is impossible to find a single marker with all of these specifications, therefore a combination of markers is required[4].

The most commonly available tests include creatinine kinase isoenzymes, lactate dehydrogenease, myoglobin, and cardiac troponins.

BIOCHEMISTRY AND DISTRIBUTION OF CARDIAC MARKERS

Cardiac markers are all myocardial proteins but they differ in their location within the myocyte, release after myocardial damage and clearance from the serum.

Creatine Kinase (CK)

Creatine kinase is an enzyme which catalyzes the formation of phosphocreatine from creatine and adenosine triphosphate (ATP)[1].Both cytosolic and mitochondrial forms of CK have been identified. The cytosolic form of the enzyme is a dimer composed of two subunits, M and B, and thus has three isoenzymes, CK-MM, CK-MB, and CK-BB.

CK-BB is the most specific to the brain and only found in the blood if the blood brain barrier is breached[5]. CK-MM accounts for the activity of CK in the skeletal muscles, while CK-MB has the most specificity to the heart muscle. The total CK-MB activity of the heart is from 10% to 20% of the total CK activity[5].

Normal skeletal muscles contain approximately 1% CK-MB. Severe muscular injury after surgery or trauma can lead to an increase of CK-MB above the reference limit in serum. This presents a diagnostic challenge in many patients. For example, persistent elevations of serum CK-MB from chronic muscle disease occur in individuals with muscular dystrophy and polymyositis, as well as healthy subjects who have vigorous exercise. This is due to the regeneration process of the muscle, with reexpression of CK-MB genes similar to those of the heart[6]. Thus distressed skeletal muscle can become like diseased heart muscle in its CK isoenzymes composition, with up to 15% CK-MB[1].

It takes at least 4 to 10 hours from onset of chest pain before CK-MB activity rise to a significant level in the blood. Peak levels occur within the first 24 hours and return to base line within 2 to 3 days.

CK-MB is commonly measured by immunoassays that use monoclonal anti-CK-MB antibodies. Excellent concordance has been shown between mass concentration and activity assays. All have detection limits of approximately 1ug/L, are 100% specific for CK-MB, and are remarkably similar in clinical performance in the diagnosis of AMI[1].

Lactate Dehydrogenase Isoenzymes

Lactate dehydrogenase (LD) is a cytoplasmic enzyme found in almost all tissues. It is a tetramer composed of two subunits, H and M, giving five isoenzymes. LD_1 is the most specific to the heart. A patient with a normal heart will have more LD_2 than LD_1, whereas a patient with cardiac damage will have a higher concentration of LD_1 than LD_2, often referred to as the "LD flip"[5]. For patients with AMI, serum total LD values become elevated at 12 to 18 hours after the onset of symptoms, peak at 48 to 72 hours, and return to below the upper reference limit after 6 to 10 days.

In patients with AMI the clinical sensitivity of the flipped ratio is > 75%, and the specificity is approximately 85% to 90%.However the measurement of LD isoenzymes often requires separation by electrophoresis, which is time consuming and involves estimation of isoenzymes activity by scanning densitometry, which is marginally precise[1].

MYOGLOBIN

Myoglobin is oxygen –binding protein of the skeletal and cardiac muscles. Its low molecular weight and cytoplasmic location probably accounts for its early appearance in blood after muscular injury, as in crush injuries or AMI. Serum methods are not able to distinguish the tissue of origin. Even minor injury to the skeletal muscles can elevate the myoglobin level, which may lead to the misdiagnosis of AMI.

Serum level of myoglobin rises as early as 1 hour after myocardial infarction. With a peak activity in the range of 4 to 12 hours (demonstrating 90% to 100% sensitivity) [1]. It is cleared rapidly so it has little clinical significance after 12 hours .The best use of myoglobin measurements after admission to the emergency department is as a negative predictor of AMI if its level remains unchanged within 2 to 4 hours of chest pain, certainty is 100% that muscle injury has not occurred[1]. The rapid disappearance of myoglobin also allows its use as an indicator of reinfarction[5].

Myoglobin should not be depended on in diagnosis of AMI in cases of renal failure, because it is normally cleared by the kidneys[5].

CARDIAC TROPONIN

The contractile proteins of all myofibrils include the regulatory protein troponins. It is a complex of three proteins, and plays a major role in the conversion of the chemical energy of adenosine triphosphate (ATP) into mechanical work. The three subunits are

–troponin C, is a dumbbell-shaped protein[7], and it is the calcium binding component[1] .It is not cardiac specific. Troponin I is the basic globular component, and is the inhibitory component. Troponin T is an asymmetric globular protein and is the tropomyosin-binding component [1, 5].

Troponin is mainly found in the myofibrils (94% to 97%), with a smaller cytoplasmic fraction (3% to 6%).

The troponin subunits exist in several isoforms. Cardiac specific troponin T (cTnT) and troponin I (TnI) isoforms have been identified. Troponin is not found in smooth muscles.

cTnI is 30 amino acids longer than the skeletal muscles form. Only one cardiac isoform has been identified. cTnI has never been shown to be expressed in normal, regenerating, or diseased human or animal skeletal muscle.[8]

cTnT has a unique 11-amino acid sequence making it cardiac specific.[1]However small amounts are made by skeletal muscle during human fetal development, in regenerating muscle, and in diseased muscle.[9]Thus cTnT has been found in skeletal muscle specimens obtained from patients with muscular dystrophy, polymyositis, and chronic renal failure [9].

CARDIAC TROPONIN ASSAY

Cardiac troponin I level is measured by monoclonal antibody-based immunoassays. It can be measured in serum, plasma, or whole blood, and the assay takes times range from 7 to 30 minutes. A qualitative whole blood rapid assay is also found commercially, which gives a positive or negative result.

The results of cTnI from different assays are variable, because of calibration and antibody differences. Currently no primary reference material is available for

manufacturers to use to standardize their assays[10, 11].The assays also fail to agree with each other because of the different epitopes recognized by the reagent antibodies used. cTnI is found in the circulation in the following three forms:

- ✓ Free
- ✓ Bound as a two subunit complex (cTnI-cTnC)
- ✓ Bound as a three-unit complex (cTnT-cTnI-cTnC)

These three forms circulate in differing degrees of degradation. Thus the different assays do not produce equivalent results, and comparison of absolute cTnI concentrations in clinical studies can not be made. Until appropriate standardization is attained, comparisons must use changes relative to each assay's respective upper reference limit[1].

Quantitative cTnT immunoassay is available. The test can be done on serum, plasma, or whole blood. The test takes around 15 minutes. Third generation reagents and antibodies are used. They do not show cross reactivity between cardiac and skeletal isoforms. It is thus 100% specific for the heart. A qualitative screening assay has also been developed with the same monoclonal antibodies used in the quantitative assay. Thus in contrast to cTnI, no standardization bias exists for cTnT.[1]

The troponin level rises after 4 to 8 hours from the onset of chest pain. This initial rise is due to release from the 5% cytoplasmic fraction. cTnI and cTnT then remain above the upper reference value for up to 5 to 10 days, respectively. This is most likely due to the release from the 95% myofibril-bound fraction. Troponin can therefore replace lactate dehydrogenase in the diagnosis of late presenting myocardial infarctions. The very low, undetectable level of troponin in patients without cardiac disease allows the use of lower discriminator values for the determination of myocardial injury and risk stratification.

CTnT differentiate patients with increased CK-MB due to skeletal muscle injury from those with myocardial injury. Furthermore, it is an excellent marker of myocardial injury in the presence of sepsis, drug-induced toxicities, chronic diseases, malignancies, hematological disorders, and noncardiac surgery.

cTnI is like CK-MB and cTnT for the sensitive detection of AMI. It is not sufficient for the early detection of AMI. It remains elevated for 3 to 5 days after the AMI.cTnI sensitivity is like that of CK-MB in the first 48 to 72 hours. Following 72 to 96 hours its sensitivity is increased. The clinical specificity of cTnI is more than 85 %.[1]Patients with severe skeletal muscle injury were found to have undetectable levels of cTnI, even when their CK-MB has reached 200ug/L and the total CK activity is up to 50,000U/L.[1]

NEW RESEARCH MARKERS

The search for the perfect marker continues. Some new markers under investigation are glycogen phosphorelase isoenzymes BB, heart fatty acid binding protein, and carbonic anhydrase.

RISK STARTIFICATION

Risk stratification is the identification of patients with an increased risk of developing AMI or cardiac death after presenting with unstable angina or minor myocardial damage. Thirty percent of these patients will progress to AMI or cardiac death within the first year of the initial presentation .[1]

Troponin measurement was found to be useful in risk stratification. This identification offers patients better diagnostic alternatives, which will further identify a sub-group of patients with refractory unstable angina who particularly can benefit from early

therapy with low-molecular-weight heparin or glycoprotein IIB and IIIA inhibitors and other interventional procedures.

Literature Review

Chest pain accounts for 2-4% of all new presentations at emergency departments in the United Kingdom .[12,13] Current best practice requires that all patients with a possible cardiac problem be admitted for at least 12-24 hours for further tests. [14,15] In the United Kingdom 30% of such patients are admitted and 70% discharged, where as in the United States around 60% are admitted. [14,16]

Among patients presenting angina fewer than 15% proceed to AMI. Of the patients with AMI presenting with prodromal symptoms, approximately two thirds, symptoms predate admission by a week or less, with a third of these having had symptoms for 24 hours or less .[1]

Identification of patients with acute chest pain at high risk for cardiovascular complications is a common and difficult challenge for clinicians and must be based initially on data for the history, physically examination, electrocardiogram, and chest radiograph. In the assessment of these patients clinical judgment plays the predominant role [17]. The presence of ST segment elevation in the ECG in highly

specific (but only about 50% sensitive [18]) for acute myocardial infarction (MI). However, many patients presenting to coronary care units have chest pain without ST elevation in the ECG. The diagnosis possibilities in these cases include: acute coronary syndrome in elevation, or non-ischemic chest pain (e.g. aortic dissection; pleurisy; pulmonary embolism; gastro-esophageal reflux, or musculo-skeletal pain).

These diagnoses are currently differentiated in many hospitals using clinical review, chest radiography, serial ECG analysis, and serial assessment of cardiac enzymes. In many cases, two or three days may elapse before a diagnosis of acute coronary syndrome can be excluded. In addition, the traditional biochemical gold-standard of CK-MB levels limited prognostic power. [19,20] Hence, many patients occupy CCU beds unnecessarily, and others are discharged only to return coronary events.

Acute myocardial infarctions are missed in about 3.5% of patients admitted to emergency departments in the United States, and such patients are subsequently discharged. IN the United Kingdom recent evidence suggest that around 6% of patients discharged from emergency department may have prognosticaly important myocardial damage.[21] Although many interventions, including drugs and surgery, can reduce mortality, patients benefit only if correctly identified[22,23,24], with missed acute myocardial infarctions is four times greater than those who are admitted to hospital.[25]

Patients who go to emergency room with chest pain without persistent ST segment elevation are common problem, and are difficult to manage on many occasions. Given the limitations of the initial elevation, the majority of these patients are admitted to the emergency medicine department, although many of them, in the end. Either have a

non-cardiac cause for their chest pain or their course is without major complications, so that they could be managed on an out-patient basis[26]. Recognition of these limitations involves the investigation of new techniques and protocols with the aim of achieving greater diagnostic efficacy, understood as practices that increase sensitivity and specificity without increasing cost and the resulting inconvenience.[27]

Diagnostic strategies applied to patients with possible cardiac chest pain in emergency departments have tow aims: firstly, the prompt identification with patients with acute myocardial infarction allowing early initiation of time dependent interventions, and, secondly, the exclusion of myocardial damage in a timely and clinically accurate manner so that patients can be discharged appropriately. The first of these is a rule-in requirement (rule in myocardial infarction). Failure of the rule-out requirement results in inappropriate discharge of patients with acute myocardial infraction.

Sensitively and specificity are measure of the clinical efficacy of a diagnostic test, where as clinical accuracy is determined by using predictive values. A test needs to be highly sensitive to be useful in a rule-out protocol. Failure to follow up patients with negative test results (verification bias) may lead to seriously misleading results.[28]

Traditionally, ruling out myocardial infraction is accomplished by combining serial measurements of cardiac enzymes (creatine kinase, aspirate transaminase, and locate dehydrogenase) with serial electrocardiograms. The sensitivity is 96.2% in patients with chest pain 24 hours after arrival at an emergency department.[14] Although accurate, this approach requires admission for a minimum of 24 hours and is therefore neither cost effective nor timely. Ideally one test would both rule out and rule in

myocardial infraction. No single test is currently and specific enough to rule out myocardial infraction in the first 6-8 hours after onset of chest pain, [29] and electrocardiography, although highly specific (77-100%), has too low a sensitivity to be used in this way.[30,31]

Patient with suspected myocardial ischemia are admitted for "screening" tests to exclude myocardial infraction, largely based on serial measurements of markers for myocardial necrosis. Historically, the markers used were non-specific enzymes released from myocardial cells and other tissues such as skeletal muscles and liver. Recently, however, extremely sensitive and specific markers have become widely available the cardiac troponins.

Cardiac troponion I and troponion T are components of the myocardial contractile apparatus. They are encoded by distinct genes, allowing the development of highly specific immunoassays.[32] Unlike other cardiac markers, the troponins are undetectable in healthy subjects, [32] so that even minor increases indicate myocardial damage.

Numerous studies have shown that the clinical sensitivity of cTnT (by use of a 0.1ug/L) is similar to that of CK-MB during the first 48 hours after the onset of chest pain.[33, 34]It has a sensitivity of about 50% to 65% from up to 6 hours after the onset chest pain. Therefore like the CK-MB it is not suitable for the early diagnosis of AMI. However cTnT remains elevated for up to 7 to 10 days after the AMI. Clinical specificity depends on how the patients are classified. It depends on whether patients with minor myocardial injury or unstable angina are included with AMI patients. If they are grouped together, the specificity of cTnT ranges from 80% to 90%.

Recently, several studies have shown that measurements of the cardiac-specific contractile proteins troponin T and I are more sensitive than CK-MB for detecting minor myocardial injury.[35, 36]In addition, they may predict events in patients with acute coronary syndromes.[19,20,37-41] Troponin T measurements are a specific and sensitive method for early and late diagnosis of acute myocardial infraction and could, therefore provide anew criterion in laboratory diagnosis of its occurrence.[42]

As cardiospecific markers, such as troponin I and creatine kinase MB are more sensitive than creatine kinase in detecting ischemic myocardial necrosis and predicting prognosis in acute coronary syndromes and coronary interventions, [43-45] in 2000 a joint committee of the European Society of Cardiology and American College of Cardiology recommended changing the diagnostic criteria for acute myocardial infarction to take account of these findings. [46]

According to the new criteria, acute myocardial infarction should be diagnosed by a raised concentration of troponin T. Troponin I, or creatine kinase in addition to typical symptoms, changes on electrocardiography, or coronary intervention. As a result, some patients previously diagnosed as having unstable angina will instead be classified as have acute myocardial infarction.

McKenna and Forfar describe how the proposed redefinition has made the measurement of cardiac specific troponin central to its diagnosis. [47] In a patient presenting with chest pain a troponin concentration above the 99th centile of normal is now sufficient to diagnose myocardial infarction, irrespective of any electrocardiographic changes. Previously, a patient had to show the development of Q waves on electrocardiography or an increase in creatine kinase activity to more than twice the upper reference limit before this judgment was made. The wide spread introduction of troponin T and troponin I measurement is an undoubted improvement,

but limitations exist with the assays, which most clinicians are unaware of and may give rise to diagnostic difficulties.

One issue concerns the use of the 99th centile of normal as the cut off point for myocardial infarction. Most assays are not sensitive enough to measure values as low as this. For example, the 99th centile for troponin T (Roche Diagnostics, Lewes, UK) is about 0.01µg/l, but the laboratory assay in routine use is unable to measure reliably below 0.03µg/l. this means that patients with troponin T concentration between 0.01µg/l and 0.03µg/l, who would be defined by the new criteria as having had a myocardial infarction, are currently being missed and included in the low risk category.

Review of 1578 subjects during the 1995 to 1998 from the Swedish Classification study showed that the use of a 0.4µg/l decision cut off point demonstrated 99% sensitivity and 94% specificity (755 AMI subjects). Within the 0.1-0.4µg/l range 43%had AMI and 57% were classified as minor myocardial damage subjects. The minor myocardial damage subjects were at increased risk of having a cardiac event at 30 days after an AMI.[1]

McKenna and Forfar mention the use of a bedside as opposed to laboratory troponin measurement, but near patient tests are less sensitive again, with the troponin T example being suitable for measurement only down to 0.01µg/l.[47]

A second issue is that troponin measurement involves immunoassay analytical techniques as opposed to the more robust enzymatic methods used with traditional cardiac markers such as creatine kinase. As Ismail and Barth pointed out, immunoassay methods can (unpredictably) lead to wrong results in some people and in the context of troponins these are likely to be difficult to identify. [48]

These and other limitations of troponin assays should not detract from the value they provide in most patients tested. They do raise concerns, however, if these tests are being used as sole means of diagnosing myocardial infarction in patients presenting with chest pain.

The initial prognostic evaluation of a patient with chest pain suggestive of ischemia can be completed within a period of 6 hours after the initiation of the chest pin, if we change the positivity limit for cTnT to 0.04ng/mL. When using the 0.1ng/mL limit, we should wait 12 hours. This evaluation includes clinical variables, ECG, and biochemical values and predicts the presence or absence of events in more than 80% of patient, so that it can be used as a summery diagnostic test .[49]

During the development of troponin assays, there has been debate about the relative value of troponin T versus troponin I testing. There are several troponin I assays available, with individual, not standardized analytical characteristics, compared to just one troponin T assay (now in its third generation), making comparisons between different clinical trials difficult[50-53]. The new third generation troponin T test has a clinically relevant cut-off point (upper limit of normal) of about 0.1µg/l and 95% sensitivity for the detection above 0.01µg/l [54]. Newer tests for troponin I show a cut-off point between 0.1µg/l and 2µg/l, with detection level around 0.007µg/l .[55]

Most commentators now agree that the troponin T and troponin I testing have similar diagnostic and prognostic power in acute coronary syndromes, and the clinicians should become familiar with the discriminator values of whichever assay is used .[56-58]

False positive evaluation of troponins I and T are (rarely) observed in patients with chronic renal failure, and troponin elevations are also seen in patients with myocarditis, pulmonary embolism, and acute heart failure .[22,23,59]

Both cTnI and cTnT were found to be raised in 10% to 30% of patients with chronic renal failure, without documented myocardial injury[60]. one 12 months study of patients undergoing chronic hemodialysis demonstrated that increases in both cTnI and cTnT predicted poor out comes (fatal infarctions)[1]. Larger studies must be performed in this population because the mortality rate within 2 years of AMI is 60% in this group .[1]

Prolonged chest pain during the 15 days prior to admission departs from the hypothesis that patients who present at admission with elevated troponin T and normal CK could constitute a subgroup of patients with AMI during the days prior to admission and who went to the emergency room with post-AMI angina that resulted in their admission. Since the kinetics of troponin T are different from those of CK-MB, these patients are able to maintain elevated cTnT for a longer time than CK-MB, and it was this discrepancy they presented in these enzymes at the time of admission .[60]

All three markers increased earlier in patients with large infarcts, and differences in reported values of sensitivity and specificity in the literature may be explained by differences in infarct size of the patients studied and the time of early sampling relative to time of onset of chest pain .[61]

An algorithm was developed using troponin I and myoglobin as adjuncts to the usual CK-MB levels that allowed for rapid and accurate assessment of patients with acute MI. it also offered physicians important input into their decision making as to how best to triage patients presenting with chest pain. Their comfort in sending home certain subgroup of patients who otherwise would have been admitted to the CCU was rewarded with a good short-term prognosis and a large cost savings to the hospital .[27]

Myoglobin is the most sensitive marker when compared to CK, CK-MB and troponin I for diagnosing patients presenting early with chest pain and non-diagnostic ECG and who subsequently develop either a ST-elevation MI or non ST-elevation MI .[62]

Cardiac markers troponin, CK-MB and myoglobin were helpful in the differential diagnosis of chest pain, even when the ECG was unremarkable or nonspecific.[17] The following ordering patterns are recommended – myoglobin (early marker) and either cTnI or cTnT (definitive mid to late markers) at presentation and at 3 to 6 hours, 6 to 9 hours, and 12 to 24 hours after presentation. If the clinical decision algorithm does not include triage within 9 hours, then myoglobin measurement is not recommended as a cost-effective test.

Despite a fall in the age adjusted prevalence of cardiovascular disease in the developed world[63], the number of patients presenting with chest pain is rising. Greater public awareness of the importance of chest pain has lowered the threshold for seeking medical help, while improvements in the ability to manage acute coronary

syndromes necessitate prompt and accurate identification of ischemic cardiac pain. Most patients who present to accident and emergency departments will have a non-cardiac pain and others, with ischemic pain, will be at low risk of serious adverse events in the short term. In contrast, many of those at high risk have no diagnostic clinical or electrocardiographic findings at presentation (about 50% of patients ultimately diagnosed as having an acute myocardial infarction, and 65% of those with unstable angina, present with non-diagnostic electrocardiogram)[64].The major challenge is therefore determining the risk of an individual patient.

There are two components to such risk. "Acute risk" is determined by the volume and severity ischemic myocardium (usually reflected in electrocardiographic changes) and the extent of myocardial injury (indicated by troponins and cardiac enzymes). "Prognostic risk" is influenced by prior cardiac damage, confounding risk factors (such as age, smoking, diabetes, and hypertension), and the extent of underlying coronary artery disease (defined by stress testing, perfusion scanning, or coronary angiography).Currently, neither form of risk is systematically evaluated .[64]

Concurrent with the increasing sensitivity of tests for cardiac necrosis, it has become clear that classifying patients with acute coronary syndromes into those with unstable angina, non-Q wave infarction, and Q wave infarction is limited in accuracy and validity[65]. A continuum of risk exists, but until recently the enzymes measured were too insensitive to reflect this. Cardiac troponins, however, provide an accurate measure of cardiac necrosis, and several large studies show that the risk of death from an acute coronary syndrome is directly related to he values of troponin I or T[66, 67].

Conversely patients with no detectable troponins have a good short term prognosis[68, 69]

The availability of such sensitive and specific markers imparts new opportunities. Instead of using blood tests merely to confirm or refute a diagnosis of acute myocardial infarction we can use cardiac troponins to triage patients with chest pain.Patients with positive values are at high risk of re(infarction) or death. They also seem to benefit most from treatments such as low molecular weight heparin and glycoprotein IIb/IIIa antagonists[70, 71], though this observation from retrospective analyses need to be confirmed prospectively. Likewise, it remains to e seen whether patients positive for cardiac troponins are those most likely to benefit from early coronary angiography and revascularization.

Patients without ST elevation and with negative cardiac troponins six or more hours after the onset of pain have an excellent short term prognosis, leading to the suggestion that they might be discharged directly from the emergency department.[68] Such a strategy has not, however, been tested prospectively. In the study by Hamm et al most patients were admitted to hospital and the favorable outcome among those with negative troponins may have been influenced by the treatment they received.[68] Nevertheless, it seems that stable patients with non-diagnostic electrocardiograms and negative markers

6-8 hours after the onset of pain need not remain in coronary care units.[69] One reasonable strategy may be to submit such patients to early predischarge exercise testing, which provides additional prognostic information reflecting the extent and severity of underlying coronary artery disease .[72]

Though cardiac troponins are undoubtedly useful in the risk stratification of patients with chest pain, they do have limitations. They take several hours to rise, peaking at 12-24 hours[65], so values on admission may be misleading. In patients initially negative for troponins a second assay should therefore be performed 6-12 hours later. In addition, values remain raised for up to 14 days[65], limiting there usefulness in diagnosing reinfarction. A further limitation relates to the standardization of, particularly, troponins I assays, which are produced by several manufacturers and may give variable results, particularly at the lower end of their range[32]. Clinicians should then familiarize themselves with the system and cut offs used locally.

As it was mentioned earlier, recent studies have suggested that positive troponins I tests are associated an increases risk of cardiac death during short-term follow up.[74] However, CK-MB and troponins I measurements are superior in clinical practice for the early risk stratification of patients presenting with acute chest pain. In non-myocardial infarction patients, both CK-MB and troponin I measurements convey independent prognostic information with regard to fatal outcome. Troponins I tests in addition to CK-MB measurements contribute to a lower rate of misdiagnoses.

Further studies have shown that cardiac troponins I plus a 2-hours myoglobin are as accurate as the combination of all three markers and performed better than CK-MB alone in detecting patients presenting late and as a predictor for complications when CK-MB was normal .[73]

Most commentors now agree that troponin T and troponins I testing have similar diagnostic and prognostic and prognostic power in acute coronary syndromes, and that clinicians should become familiar with the discriminator values of whichever assay is used[56- 58].

The combination of baseline troponins I with different parameters resulted in a higher sensitivity of up to 98%, with a similar predictive accuracy, but a lower specificity. Additive measurements o cardiac troponins I at 6 hours to baseline cardiac troponins T and I proved to be the best combination for prediction of subsequent cardiac events. Changes in cut-off levels of cardiac markers and inflammatory parameters results in a high accuracy of risk stratification in patients with chest pain. Combination of these measurements might further help in the identification of patients who would benefit from early coronary revascularization .[74]

The availability of such sensitive and specific markers imparts new opportunities. Instead of using blood tests merely to confirm or refute a diagnosis of acute myocardial infarction we can use cardiac troponins to triage patients with chest pain. Patients with positive values are at high risk of (re)infarction or death. They also seem to benefit most from treatments such as low molecular weight heparin and glycoprotein IIb/IIIa antagonists[70,71], though this observation from retrospective analyses needs to be confirmed prospectively. Likewise, it remains to be seen whether patients positive for cardiac troponins are those most likely to benefit from early coronary angiography and revascularization.

Comparison of a troponins-based acute chest pain protocol against standard management for patients with acute coronary syndrome found that troponins based management allowed earlier discharge in approximately 50% of patients (the low risk group) with no excess of adverse events compared to standard management. It also identified a group of patients (about 25% o patients) at a moderate risk of cardiac events, for whom early angiography and intervention could be considered.

Finally, the troponins protocol identified a high-risk group (abut 25% of patients) more accurately than standard management for whom aggressive medical therapy and inpatient investigation/ revascularization would be appropriate. We believe such a protocol should not be considered a replacement for careful clinical assessment, but rather an adjunct to it. This adds to the accumulating evidence in favor of troponins evaluation as part of the diagnosis and risk stratification of acute coronary syndrome .[75]

OBJECTIVES

The aim of the study was to investigate the usefulness and accuracy of troponin I in:

- Early diagnosis of myocardial infarction.
- Prediction of future adverse cardiac events.

Materials and methods

Study design

This is a prospective observational hospital based study. It was conducted at Elshaab Teaching Hospital, which is the largest cardiac centre in Sudan. The study started in May 2005 and ended in July 2005.

Study population

The study population was any patient presenting with acute chest pain to the casualty during the period of the study. Sixty patients and thirty controls were included in the study.

Inclusion criteria

Any patient presenting with acute chest pain (not more than two weeks) to the casualty of Elshaab Teaching Hospital.

The controls were apparently healthy hospital staff matching with age and sex to the studied population.

Exclusion criteria

- Chest pain for more than two weeks.
- Traumatic causes of chest pain.
- Patients with renal insufficiency (creatinine >2 mg/dL).
- Patients with left bundle branch block.

Tools and methods

Consent

Verbal consent was taken from the hospital's administration, and the patients.

Questionnaire (Appendix I)

Clinical diagnosis

The patients were examined by the doctors on duty. ECG and creatinine were requested for every patient. The diagnoses were made by the registrar on duty. An 'ischemic ECG' was ST depression >1 mm in any lead, or abnormal T-wave inversion. Patients with established left bundle branch block on the ECG were considered to have a 'non-ischemic' ECG for the purposes of this study.

Patients with ischemic ECG and typical chest pain, occurring at rest and constant, were diagnosed as acute myocardial infarction. Patients with typical chest pain also occurring at rest but without ECG changes are diagnosed as unstable angina.

Any patient not presenting with the above was diagnosed as **others**, which is non cardiac cause for the chest pain.

Methods of blood collection

Blood was collected under possible aseptic conditions from the anticubital fossa veins 3 milliliters of blood were taken using a disposable plastic syringe and put in a plain container. This was centrifuged after clotting and the serum is separated in another plain container and stored in a -20ºC freezer.

Serum Troponin I

This was done by the Immulite Analyzer using troponin I reagent for in vitro quantitative determination of cardiac troponin I.

The principle of the procedure is a chemiluminescence immunometric assay.

Materials used

- Troponin I Test Units (LTI1): each barcode-labeled unit contains one bead coated with monoclonal murine anti-troponin I antibody.
- Troponin I Reagent Wedge (LTI2): With barcode 6.5mL of alkaline phosphatase (bovine calf intestine) conjugated to polyclonal goat anti-troponin I antibody in a buffer.

- Troponin I Adjustors (LTIL, LTIH): Two vials (Low and High) of lyophilized troponin I in a nonhuman serum matrix.
- LSUBX: Chemiluminescent substrate.
- LPWS2: Probe Wash Module.
- LKPM: Probe Cleaning Kit.
- LCHx-y: Sample cup holders (bar-coded).
- LSCP: Sample Cups (disposable).
- CCCM: A bi-level, nonhuman serum-based Cardiac Marker Control Module, containing troponin I as one of three different constituents.

PROCEDURE (Appendix II)

Expected Values

A troponin concentration of 1ng/mL or more is considered abnormal.

QUALITY CONTROL

Controls with two levels high and low of troponin I were used.

LIMITATIONS

The assay yields lower values when used with EDTA plasma.

Heterophilic antibodies in human serum can react with the immunoglobulins included in the assay components causing interference with the in vitro immunoassays.

Samples from patients routinely exposed to animals or animal serum can demonstrate this type of interference potentially causing an anomalous result. These reagents have been formulated to minimize the risk of interference; however, potential interaction between rare sera and test components can occur.

For diagnostic purposes the results obtained from this assay should always be used in combination with the clinical data.

PERFORMANCE DATA

Analytical Sensitivity: 0.1ng/mL.

Specificity: The antibodies are highly specific to troponin I.

Calibration Range: Up to 180ng/mL.

FOLLOW UP

Patients were monitored during the index admission for adverse cardiac events. Following discharge, all patients were contacted after 30 days from presentation by telephone. Adverse events were confirmed by reference to hospital notes.

DATA ANALYSIS

Data was analyised using SPSS computer program.

CHAPTER THREE

RESULTS

Figure 1: Distribution of the studied population

This figure shows that 25 patients (41.7%) of the cases presenting with acute chest pain to the casualty were males and 35 patients (58.3%) were females.

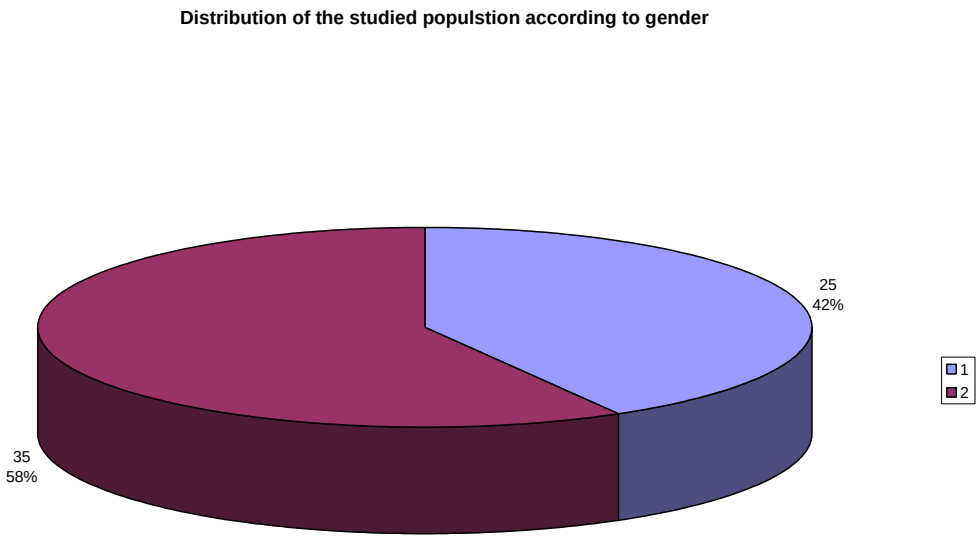

Figure 2: Distribution of the studied population according to age.

This figure shows that 32 patients (53.3%) were between 31 and 59 years and 22 patients (36.7%) were 60 years or more.

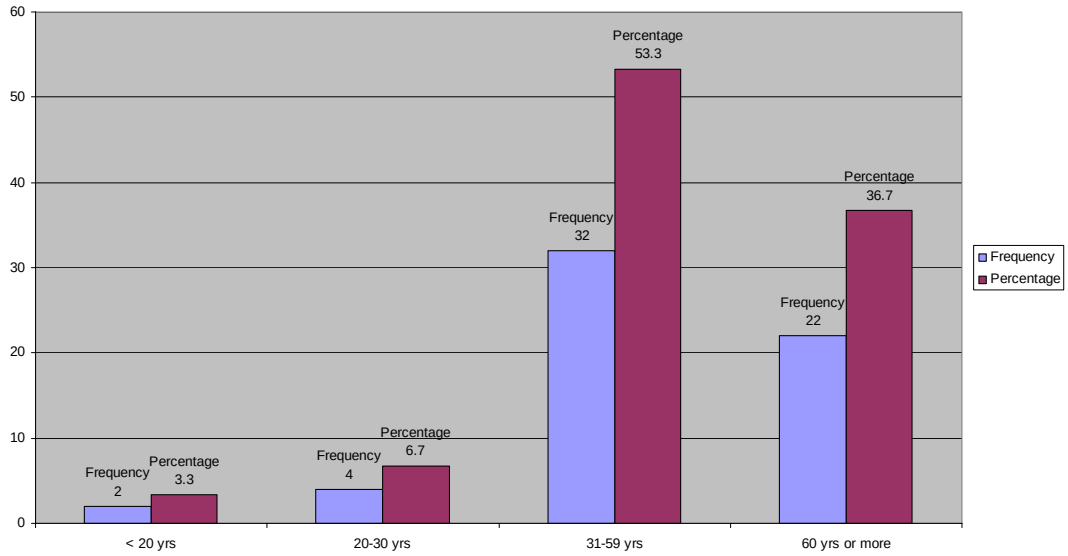

Figure 3: Distribution of the studied population according to the time of presentation from onset of chest pain.

This figure shows the duration of time the patients took before presenting to the casualty. Thirty six patients (60%) presented between 6 hours and 5 days.

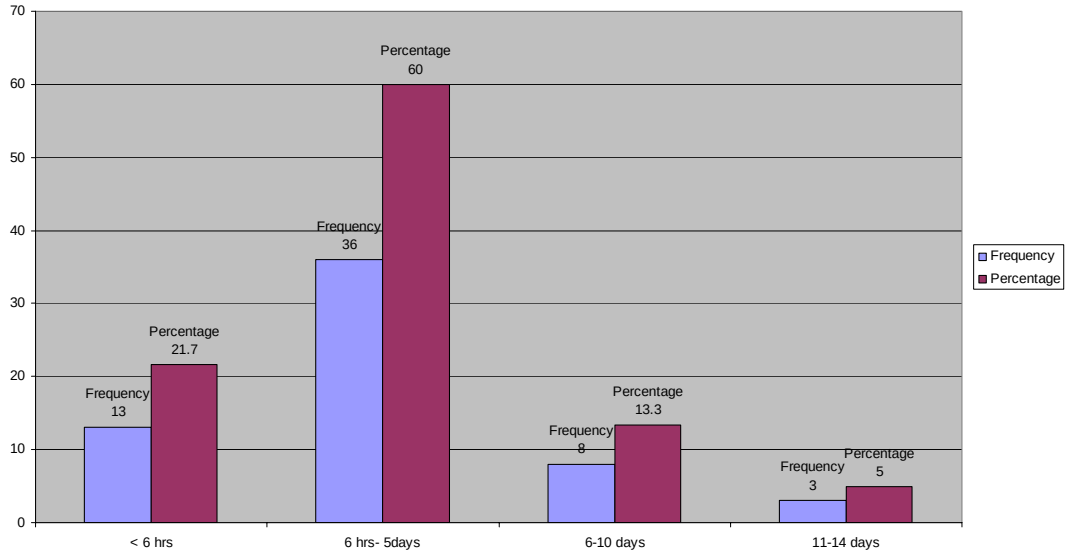

Figure 4: Distribution of the studied population according to the diagnosis.

This figure shows the diagnoses of the patients studied. Twenty one patients (35%) had myocardial infarction. Twelve patients (20%) had unstable angina and 27 patients (45%) had other conditions.

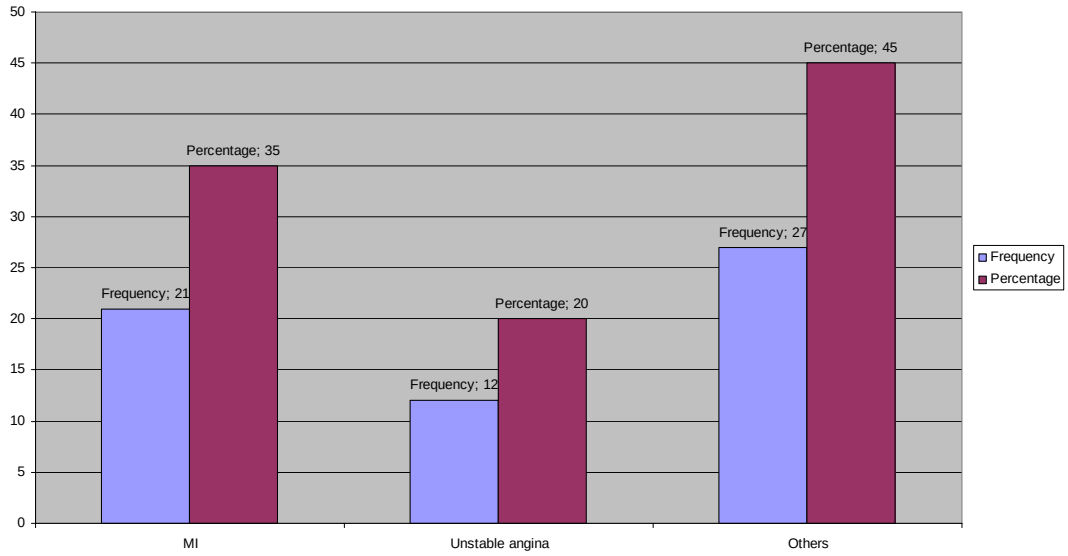

Figure 5: Distribution of the study population according to the outcome after one month.

After one month from presentation, 51 patients (85.0%) had no complication. Five patients (8.3%) had passed away, three patients (5.0%) had a reinfarction, and only 1 patient (1.7%) could not be found.

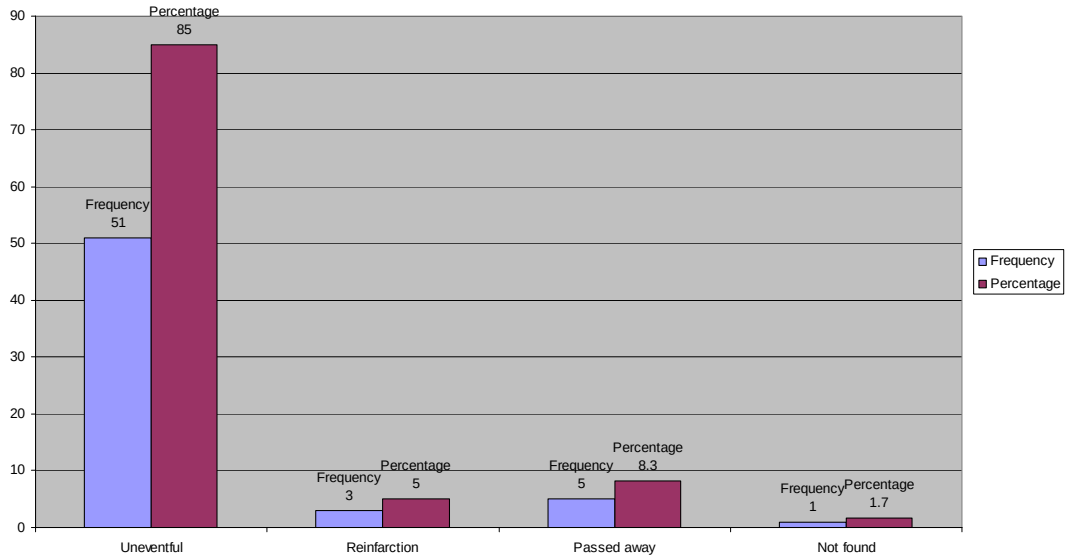

Figure 6: Distribution of patients according to the troponin I concentration.

When the cut off value of troponin is taken as 1.0ng/mL, 20 patients (33.3%) had a troponin concentration >1.0ng/mL while 40 patients (66.7%) had troponin concentration <1.0ng/mL

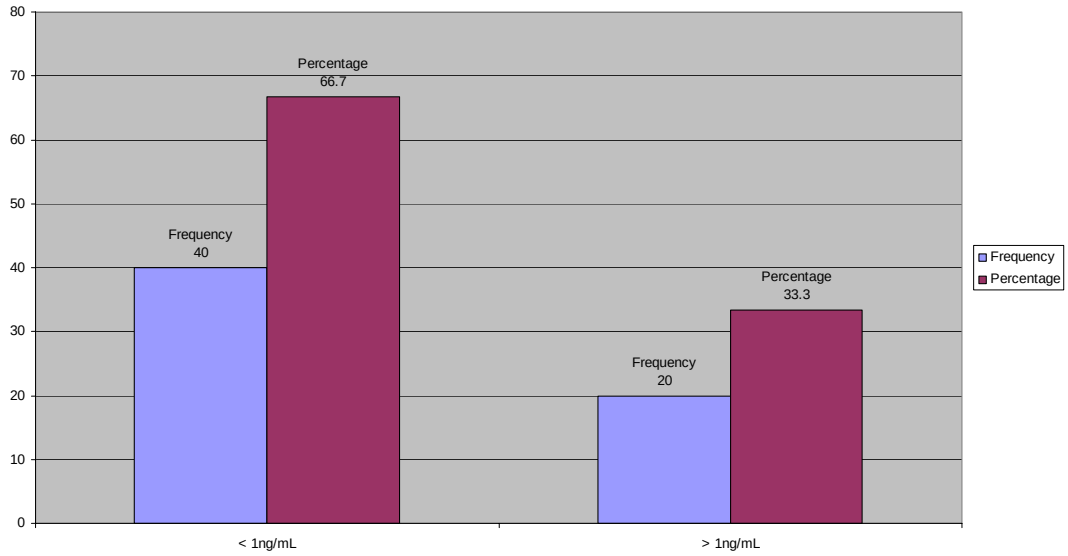

Table 1: Relation between the troponin I concentration and the diagnosis.

Forty patients (66.7%) had a troponin concentration less than 1.0ng/mL. Nine patients (15%) had MI, 15% (9 patients) had unstable angina and 22 patients (36.70%) had other diagnoses. Twenty patients (33.3%) had a troponin concentration > 1.0 ng/mL. Of these 12 patients (20%) had MI, 3 patients (5%) had unstable angina,

and 5 patients (8.3%) had other diagnoses. There is a statistically significant relationship.

Diagnosis	Troponin <1.0 ng/mL	Troponin > 1.0 ng/mL	Total
MI	9 (15%)	12 (20%)	21 (35%)
Unstable angina	9 (15%)	3 (5%)	12 (20%)
Others	22 (36.7%)	5 (8.3%)	27 (45%)
Total	40 (66.7%)	20 (33.3%)	60 (100%)

P=0.015

Table 2: Distribution of the studied population according to grouping of the troponin levels.

This table shows that 34 patients (56.7%) had a troponin value of 0.2ng/mL or less.Six patients (10%) had a value of 0.3 up to 1.0 ng/mL. Thirteen patients (21.7%) had a troponin concentration of 1.1 ng/mL and up to 5.0 ng/mL. One patient (1.7%)

had a value of 5.1 ng/mL up to 10.0 ng/mL .Finally 6 patients (10%) had a troponin level more than 10.0 ng/mL.

Troponin	0.2ng/mL or less	0.3 to1.0 ng/mL	1.1 to 5.0 ng/mL	5.1 to 10.0 ng/mL	> 10.0 ng/mL	Total
Frequency	34	6	13	1	6	60
Percentage	56.7%	10.0%	21.7%	1.7%	10.0%	100.0%

Figure 7: Distribution of patients with a troponin I concentration < 1.0ng/mL according to the diagnosis

Among the patients with a troponin concentration <1.0 ng/mL, 9 patients (22.5%) had MI, 9 patients (22.5%) had unstable angina, and 22 patients (55.0%) had other diagnoses.

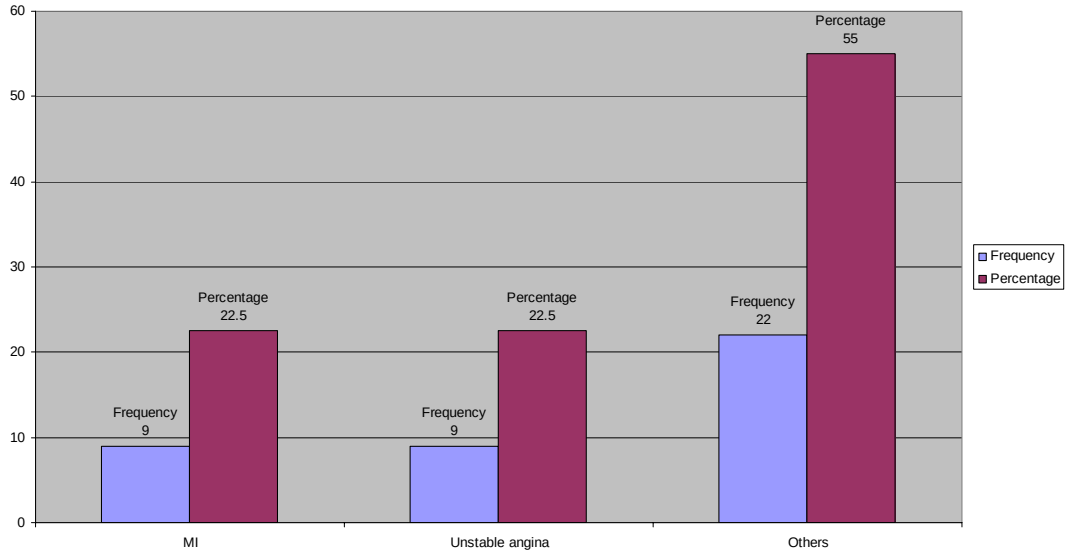

Figure 8: Distribution of patients with a troponin I concentration >1.0ng/mL according to diagnosis

Among the patients with a troponin concentration > 1.0 ng/mL, 12 patients (60%) had MI, 3 patients (15%) had unstable angina, and 5 patients (25%) had other diagnoses.

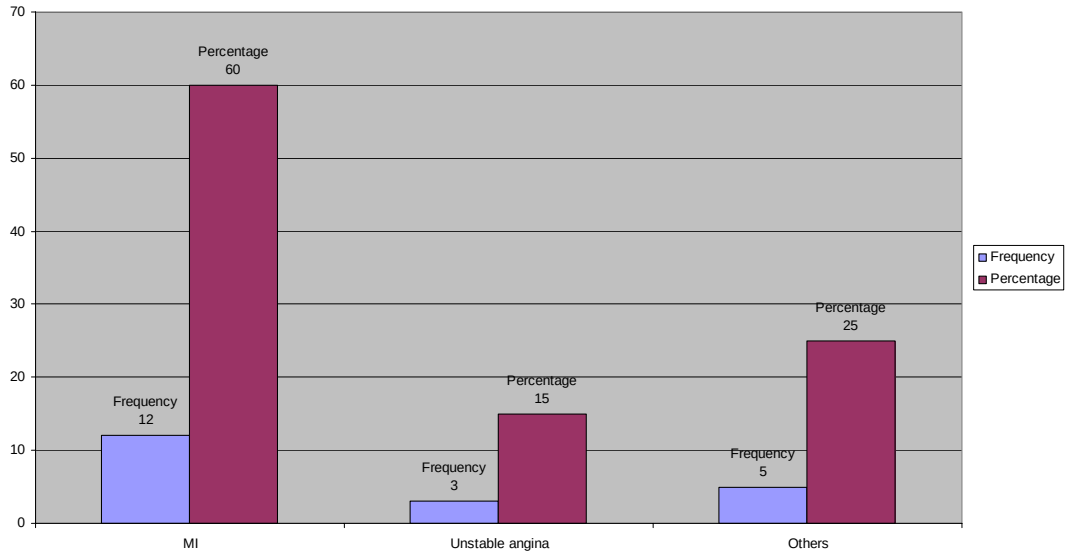

Table 3: Distribution of the troponin I concentration according to the time of presentation

Forty patients (66.7%) of the studied population who had a troponin concentration <1.0ng/mL. 9 patients (15.0%) presented less than 6 hours, 22 patients (36.7%) presented between 6 hours and 5 days, 8 patients (13.3%) presented between 6 days and 10 days, and 1 patient (1.7%) presented between 11 days and 14 days. 20 patients (33.3%) of the studied population had a troponin concentration >1.0ng/dl. 4 patient

(6.7%) presented less than 6 hours, 14 patients (23.3%) presented between 6 hours and 5 days. This was not statistically significant.

	<6hours	6 hours- 5 days	6 days- 10 days	11 days- 14 days	Total
Troponin <1.0ng/mL	9 (15.0%)	22 (36.7%)	8 (13.3%)	1 (1.7%)	40 (66.7%)
Troponin >1.0mg/dl	4 (6.7%)	14 (23.3%)	0 (0%)	2 (3.3%)	20 (33.3%)
Total	13 (21.7%)	36 (60.0%)	8 (13.3%)	3 (5.0%)	60 (100%)

P= 0.11

Figure 9: Distribution of patients with a troponinI concentration < 1.0ng/mL according to the time of presentation.

Nine patients (22.5%) presented less than 6 hours from onset of chest pain. Twenty patients (55.0%) presented between 6 hours and 5 days.

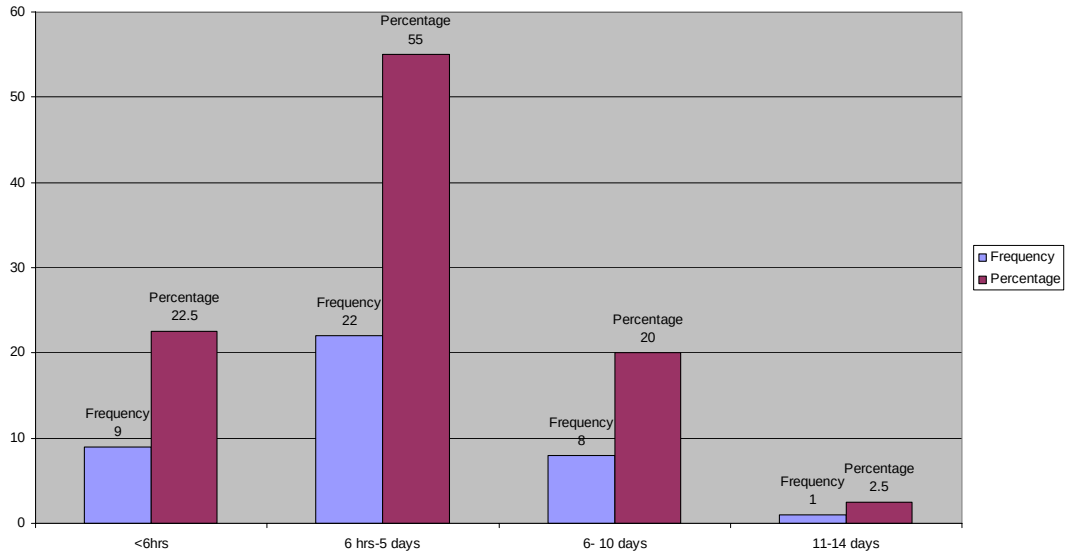

Figure 10: Distribution of patients with a troponin I concentration > 1.0ng/mL according to the time of presentation from the onset of chest pain.

Four patients (20.0%) presented less than 6 hours. Fourteen patients (70.0%) presented between 6 hours and 5 days.

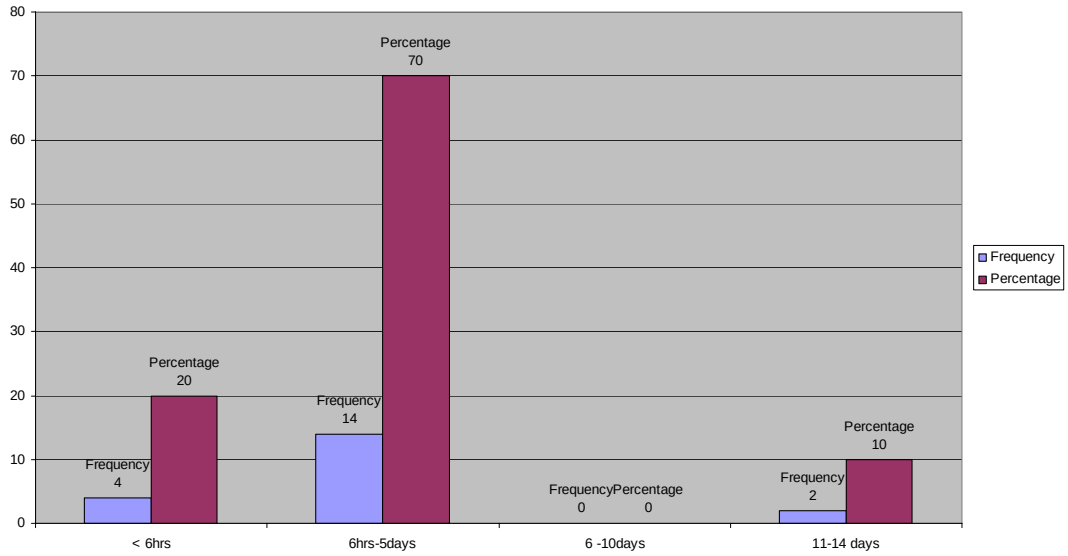

Table 4: Distribution of the studied population according to the troponin I concentration and the outcome.

Out of the whole study population 40 patients (66.7%) had a troponin concentration <1.0ng/mL. Thirty seven patients (61.6%) had an uneventful outcome, 20 patients (33.3%) had a troponin concentration >1.0ng/mL, 14 patients (23.3%) had an uneventful outcome, and 4 patients (6.7%) passed away. This was not statistically significant although the P value was very near to 0.05.

	Uneventful	Reinfarction	Passed	Not found	Total
Troponin < 1.0ng/mL	37 (61.6%)	1 (1.7%)	1 (1.7%)	1 (1.7%)	40 (66.7%)
Troponin >1.0ng/mL	14 (23.3%)	2 (3.3%)	4 (6.7%)	0 (0%)	20 (33.3%)
	Total	5 (8.4%)	3 (5.0%)	1 (1.7%)	60 (100%)

P= 0.053

Figure 11: distribution of the patients with a troponin I concentration <1.0ng/mL according to the outcome.

37 patients (92.5%) had an uneventful outcome, 1 patient (2.5%) had a reinfarction, 1 patient (2.5%) passed away, and 1 patient (2.5%) was not found.

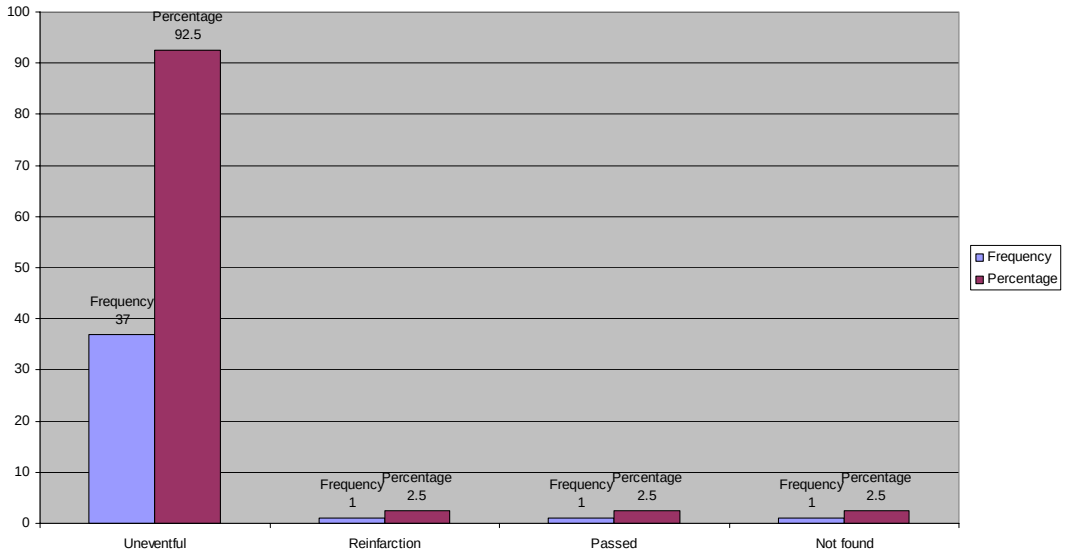

Figure 12: Distribution of the patients with a troponin concentration >1.0ng/mL accordion to the outcome.

14 patients (70.0%) had an uneventful outcome, 2 patients (10.0%) had a reinfarction, and 4 patients (20.0%) passed away.

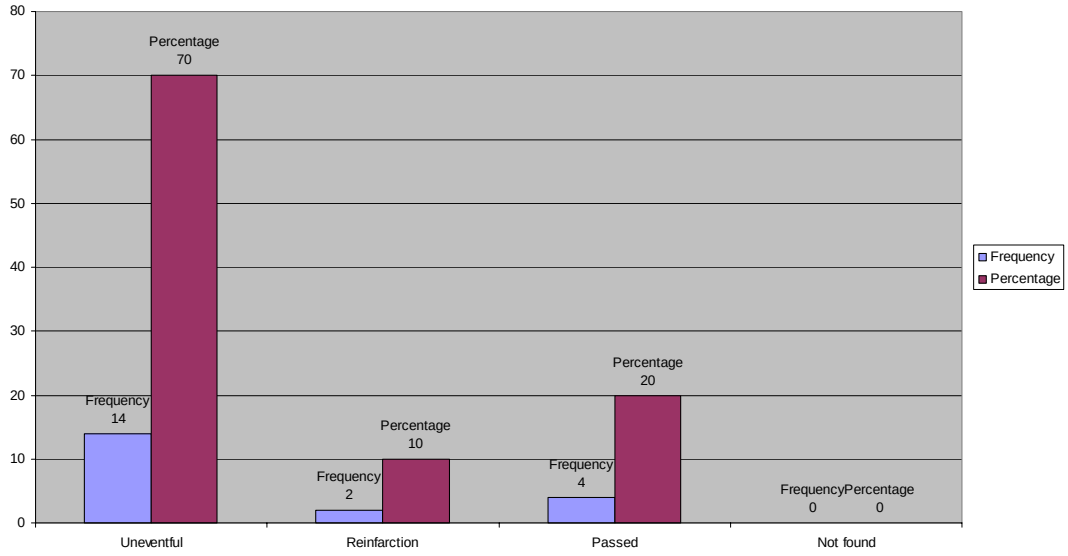

Table 5: Distribution of the studied controls according to sex

This table shows that 10 patients (50.0%) of the controls were males and 10 (50.0%) were females.

	Male	Female	Total
Frequency	10	10	30
Percentage	50.0%	50.0%	100.0%

Table 6: Distribution of the studied controls according to age.

2 patients (6.7%) were less than 20 years. 2 patients (6.7%) were between 20 and 30 years, 12 patients (40.0%) were between 31 and 59 years and 14 patients (46.6%) were 60 years or more.

	Less than 20 years	20-30 years	31-59 years	60 years or more	Total
Frequency	2	2	12	14	30
Percentage	6.7%	6.7%	40.0%	46.6%	100.0%

All the studied controls had a troponin concentration < 0.2ng/mL.

CHAPTER FOUR

DISCUSSION

This study evaluated the effectiveness of troponin I in the assessment of patients presenting with acute chest pain.

The studied population showed an equal rate of presentation to the hospital between males and females, with a slight female's predominance.

The most common age group presenting with chest pain was between 31-59 years followed by those above 60 years.

Most of the patients did not present immediately after the onset of symptoms, the majority presented between 6 hours and 5 days (figure 3). This goes with the trend in the literature[1], and it underscores the value of troponin I in identification of patients with acute coronary syndrome, because this is the best time to test for troponin I level .[1]

Among the patients presenting with acute chest pain, the majority had diagnoses other than acute coronary syndrome. This might reflect an increased awareness of public about the importance of chest pain and ischemic heart disease[63] and so necessitating the need for a rapid, sensitive and cost effective means of evaluating these patients[27], and identification of those with acute myocardial infarction[28], so as to be managed appropriately.

The troponin I level needed for the diagnosis of acute myocardial infarction is 1.0ng/mL[1]. This identified more than half of the patients diagnosed as having acute myocardial infarction by clinical features and ECG in the study (table 1). The rest had a negative troponin I test. This was related to the time at which the test was done after the onset of symptoms. Four of these patients presented less than 6 hours after their symptoms, two presented more than ten days later but two patients their negative result was unexplainable. Patients with acute myocardial infarction presenting too early or too late will have a negative troponin.

It was clear that most of the patients in the study who had an acute chest pain for reasons other than an acute coronary syndrome had a negative troponin test (<1.0ng/mL). This makes troponin I sensitive in ruling out patients presenting with chest pain and their early discharge.

Some of the patients in the study had a troponin concentration more than 1.0mg/dl although they were not diagnosed as having a myocardial infarction. These patients might have had a non ST segment myocardial infarction and so could not be identified by the clinical history and the ECG. These patients needed to be admitted and followed up, but when the troponin concentration was measured it was found to be diagnostic of myocardial infarction. As McKenna and Forfar[47] described, chest pain and a high troponin level should be sufficient to diagnose acute coronary syndrome, irrespective of the ECG changes. Accordingly patients with a high troponin concentration and ECG changes pointing towards unstable angina should be diagnosed and managed as having an acute myocardial infarction. Young GP, et al[73] stated that with the additional knowledge of troponin I values, it could be demonstrated that certain cases were misclassified as having noncardiac chest pain.

Similarly patients with out diagnostic ECG changes of acute coronary syndrome, but a high troponin, should be offered further diagnostic investigations, interventional measures, and close follow up. This will reduce the number of patients discharged with missed acute myocardial infarction[16,76,77], identifies those at risk of developing an acute coronary syndrome in the future and so benefit from early cardiac revascularization .[74]

In the study patients with myocardial infarction had different levels of troponin (table 2). This could be explained by the different times of presentation, and might be related to the size of the infarct[61].Patients with the high troponin concentrations in the study were not found to have statistically significant worse out comes (reinfarction or death).However, several large studies found that the risk of death from an acute coronary syndrome is directly related to values of troponin I or T[66, 67]. Young GP, et al[73] in Germany also found that in patients without myocardial infarction on

admission, 10.5% with positive troponin I tests died compared to 1.6% with negative tests. He concluded that troponin I convey independent prognostic information with regard to fatal outcome. Lim J et al[62]in Singapore study also reached the conclusion that patients with an elevated troponin I level are at higher risk of an adverse clinical event.

This contradiction between the results in the study and the literature might be due to the small sample size and the small percentage of those with a high troponin concentration and acute coronary syndrome.

All the controls in the study had an undetectable troponin I (<0.2ng/mL).This was also noticed by Hamm[78], and it is this fact that makes troponin highly sensitive and specific in the diagnosis of acute myocardial infarction.

One patient in the study had a normal troponin concentration but still she passed away. The cause of death was not cardiac in origin.

CONCLUSION

- This study concluded that troponin I is valuable in the diagnosis and exclusion of acute myocardial infarction.
- The time of presentation after the onset of chest pain is not related to the change in the troponin level.
- High troponin level is not associated with a worse outcome.

RECOMMENDATIONS

- Introducing troponin assays in all the cardiology casualties for prompt diagnosis and risk stratification of acute coronary syndromes.
- Conducting larger studies to relate the time of presentation and the outcome to the troponin concentration in patients with acute coronary syndrome.

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APPENDIX I

Value of Troponin in diagnosis of MI
&
Risk Stratification
Among Sudanese Patients presenting to Alshaab Teaching Hospital in the period between 5th May-5th July-2005.

Date:…….

Name:……Tel:……
…

Age:……
……

Sex:……
…

Duration of chest pain:
<6hours……6hours-5 days……..
6 days- 10 days……...11 days- 14 days ,

Clinical Diagnosis with ECG: MI …….
Angina…….. Others…….
…….

SerumTroponin :……

<u>Outcome after one month:</u>

Uneventful…….Infarction/Reinfarction……
…..Death……. Others…….

APPENDIX II